

Etiology and predictors of hereditary angioedema cluster-attacks despite pharmaceutical treatment

U. Strassen¹, M. Wirth¹, Z. Zhu¹, J. Hahn², J. Greve², E. Ebert¹, F. Johnson¹

¹Department of Otorhinolaryngology, Technische Universität München, Germany

²Department of Oto-Rhino-Laryngology, Head and Neck Surgery, Ulm University Medical Center, Germany

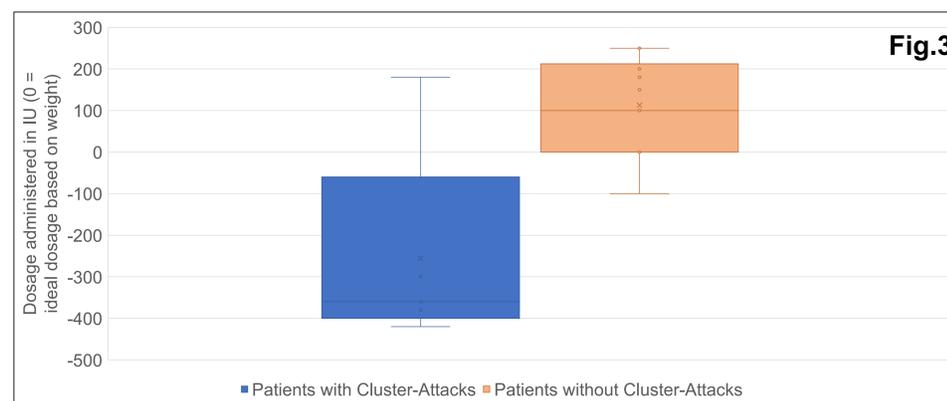
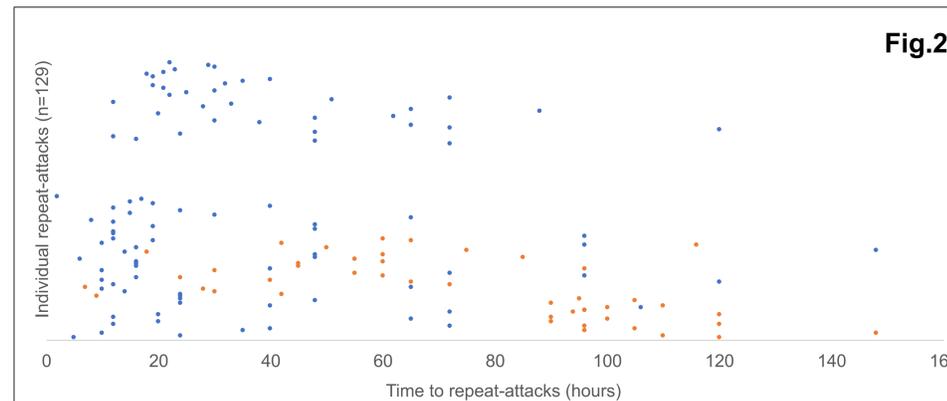
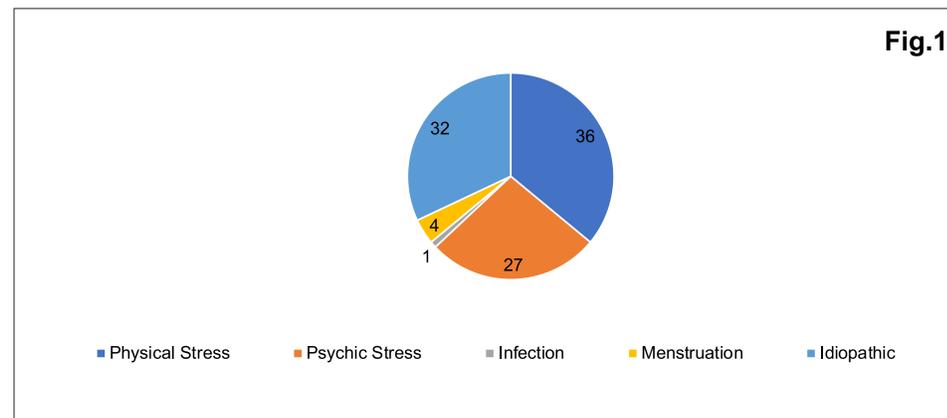
Introduction:

Hereditary angioedema is a disease which leads to recurrent swelling of the skin and mucous membranes including the upper airway tract. Besides being deadly, these attacks can be debilitating, leading to a poor quality of life for patients. Clinicians are occasionally confronted with patients who have recurrent attacks despite treatment with C1-Inhibitor concentrate (C1-INH) or Icatibant. The goal this study is to investigate repeat attacks which re-occur within a week ("cluster-attacks") after treatment, to determine why they occur and with what factors they may be associated with, and hereby prevent their occurrence.

Methods:

We conducted a multi-center mixed retrospective/prospective study data acquisition of all documented attacks from our HAE patient collective (n=132) from 2015 to 2018.,

Sources:
¹ Caballeo T, J. Investig Allergol Clin Immunol 2016
² Zotter Z, Orphanet J Rare Dis 2014
Funding:
 Pharming Group



Results:

85% of our patients agreed to participate in the study. 11% of these patients had cluster-attacks, with a total of 126 cluster-attacks. Approximately 66% of these were caused by exogenous stimuli (Fig.1).

Cluster-attacks were encountered by 7% of patients who were receiving a prophylactic therapy and 14% of patients who were receiving an on-demand therapy.

A significantly lower time to repeat attack could be found for patients who received Icatibant as compared to those who used C1-INH (Fig.2).

80% of patients who were receiving a prophylactic treatment were underdosing their C1-INH therapy (according to the recommended dosage per bodyweight in U). Fig.3 shows the administered dose in relation to the ideal dose for patients with and without cluster attacks.

Discussion:

The percentage of patients who had attacks as a result of exogenous triggers was higher in the cluster-attack group (64%) as compared to the general HAE population (30-42%¹⁻²). Repeat attacks are therefore strongly associated with external triggers.

Patients who were receiving a prophylactic treatment who had cluster-attacks are highly likely to have been underdosing, which may explain repeated attacks despite treatment.

Shorter time to cluster-attacks in patients treated with Icatibant may be explained by the shorter plasma half-life of the medication compared to C1-INH.

In patients who are prone to cluster-attacks a prophylaxis should be considered.